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Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Anne Corrigan

Timestamp: [year=2011; month=4; day=22; hr=9; min=53; sec=48; ms=413;]

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Reviewer Comments:

<120> Method for detecting LDL receptor gene mutations associated with

Please complete the above "<120>" response: "Method for detecting LDL receptor gene mutations associated with Familial Hypercholesterolemia"

(Sequence 1 has many errors. Errors shown below)

<220>

<221> gene

<223> n at position 35360 represents aau, aac or aat

<220>

<221> gene

<223> n at position 35361 represents aau, aac or aat

Errors above: a single "n" can only represent a single nucleotide, not a codon.

cctctgcctc ctgggttcaa gcgattttcc tgctcagcc tcccgagtag ctgggattac 8160
aggtgcttgc caccataccc ggctaatttt gtatttttag tagagacggg gttacgcca 8820

The "8820" above is incorrect: the cumulative nucleotide total should be "8220". Please check all succeeding cumulative nucleotide totals in Sequence 1 for accuracy: mistakes have been noted.

actgcctggc agaggctgcg agc atg ggg ccc tgg ggc tgg aaa ttg cgc 15350

Met Gly Pro Trp Gly Trp Lys Leu Arg

-21 -20

-15

tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca g gtaaggcttg 15400

Trp Thr Val Ala Leu Leu Leu Ala Ala Ala Gly Thr Ala
 -10 -5 -1 1

The above misaligned amino acids are samples of TAB codes appearing throughout Sequence 1: please remove all TAB codes, and align the amino acids and amino acid numbers, properly. Do not show TAB codes in the sequence listing.

Asp Ile Asp Glu Gys Gln Asp
 335
 ccc gac acc tgc agc cag ctc tgc gtg aac ctg gag ggt ggc tac aag 36686
 Pro Asp Thr Cys Ser Gln Leu Cys Val Asn Leu Glu Gly Gly Tyr Lys
 340 345 350 355
 tgc cag tgt gag gaa ggc ttc cag ctg gac ccc cac acg aag gcc tgc 36734
 Cys Gln Cys Glu Glu Gly Phe Gln Leu Asp Pro His Thr Lys Ala Cys
 360 365 370
 aag gct gtg g gtgagcacgg gaaggcggcg ggtgggggcg gcctcacccc 36784
 Lys Ala Val
 375

Besides TAB codes causing misalignment, "Gys" (in the top amino acid row above) is an invalid amino acid designator.

<210> 2
 <211> 24
 <212> DNA
 <213> artificial sequence
 <220>
 <223> Ex1F

Please remove the extra blank space between "Artificial" and "Sequence" in the above "<213>" response. Only one blank space should separate "Artificial" and "Sequence". Same error in many subsequent sequences.

As an explanation of "<213> Artificial Sequence", the above "<223>" response needs more information regarding the source of the genetic material. If this is a primer, please add that to the "<223>" response. Same type of response in subsequent sequences.

<210> 90

<211> 20
<212> DNA
<213> artificial sequence

<220>
<223> probe

<400> 90

cactctcggg cccctaccc 20

Although the above "<211>" response is "20", only 19 nucleotides are shown. The second group of nucleotides totals "9".

<210> 232
<211> 25
<212> DNA
<213> artificial sequence

<220>
<223> probe

<400> 232

ttgtccttgc agtcggggcc acta 25

Although the above "<211>" response totals "25", only 24 nucleotides are shown. The last group totals "4".

Suggestion: please consult the Sequence Rules for valid format.

To correct the sequence listing errors noted in this report - The recommended method for correction of errors is to access the sequence listing working file using the software program in which the listing was originally prepared, e.g., the project file in PatentIn, make any necessary corrections within that program, then generate a new sequence listing file. Use of a word processing program to correct errors directly in the original sequence listing file is strongly discouraged, since such programs often introduce unintended changes to the sequence listing, rendering the listing unacceptable. When the working file or original program is not available for correction, then use of a common

or plain text-only editor, such as NotePad, to edit the original
sequence listing file may suffice.

Application No: 10542937 Version No: 4.0

Input Set:

Output Set:

Started: 2011-04-13 11:37:43.725
Finished: 2011-04-13 11:38:01.699
Elapsed: 0 hr(s) 0 min(s) 17 sec(s) 974 ms
Total Warnings: 277
Total Errors: 414
No. of SeqIDs Defined: 259
Actual SeqID Count: 259

Error code	Error Description
E 254	The total number of bases conflicts with running total, Input: 8820, Calculated : 8220 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
E 254	The total number of bases conflicts with running total, Input: 18940, Calculated : 19840 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 20190, Calculated : 20200 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 22700, Calculated : 22720 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (61)
E 254	The total number of bases conflicts with running total, Input: 28210, Calculated : 28260 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
E 254	The total number of bases conflicts with running total, Input: 39861, Calculated : 30861 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)

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Actual SeqID Count: 259

Error code	Error Description
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E 323	Invalid/missing amino acid numbering SEQID (1) POS (136)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (140)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (141)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (145)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (146)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (150)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (151)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (155)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (156)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (160)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (161)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (165)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (166)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (170)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (171)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (175)
E 323	Invalid/missing amino acid numbering SEQID (1) POS (176)
E 323	Invalid/missing amino acid numbering SEQID (1)at Protein (180) This error has occurred more than 20 times, will not be displayed
E 254	The total number of bases conflicts with running total, Input: 33271, Calculated : 33171 SEQID(1)
E 342	'n' position not defined found at POS: 35360 SEQID(1)

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Error code	Error Description
E 342	'n' position not defined found at POS: 35361 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
E 330	Invalid protein , found in SEQID(1) POS (358)Invalid Protein:Gys
W 333	tabs used in amino acid numbering SEQID (1)
E 254	The total number of bases conflicts with running total, Input: 37984, Calculated : 37983 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38044, Calculated : 38043 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38104, Calculated : 38103 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38164, Calculated : 38163 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38224, Calculated : 38223 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38284, Calculated : 38283 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38344, Calculated : 38343 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38399, Calculated : 38398 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38447, Calculated : 38446 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38495, Calculated : 38494 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38543, Calculated : 38542 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38594, Calculated : 38593 SEQID(1)
E 254	The total number of bases conflicts with running total, Input:

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Error code	Error Description
	This error has occurred more than 20 times, will not be displayed
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 333	tabs used in amino acid numbering SEQID (1)
W 402	Undefined organism found in <213> in SEQ ID (2)
W 402	Undefined organism found in <213> in SEQ ID (3)
W 402	Undefined organism found in <213> in SEQ ID (4)
W 402	Undefined organism found in <213> in SEQ ID (5)
W 402	Undefined organism found in <213> in SEQ ID (6)
W 402	Undefined organism found in <213> in SEQ ID (7)
W 402	Undefined organism found in <213> in SEQ ID (8)
W 402	Undefined organism found in <213> in SEQ ID (9)
W 402	Undefined organism found in <213> in SEQ ID (10)
W 402	Undefined organism found in <213> in SEQ ID (11)
W 402	Undefined organism found in <213> in SEQ ID (12)
W 402	Undefined organism found in <213> in SEQ ID (13)
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Input Set:

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No. of SeqIDs Defined: 259
Actual SeqID Count: 259

Error code	Error Description
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W 402	Undefined organism found in <213> in SEQ ID (17)
W 402	Undefined organism found in <213> in SEQ ID (18)
W 402	Undefined organism found in <213> in SEQ ID (19)
W 402	Undefined organism found in <213> in SEQ ID (20)
W 402	Undefined organism found in <213> in SEQ ID (21) This error has occurred more than 20 times, will not be displayed
E 253	The number of bases differs from <211> Input: 20 Calculated:19
E 253	The number of bases differs from <211> Input: 25 Calculated:24

SEQUENCE LISTING

<110> Mata Lopez, Pedro
 Mozas Alonso, Pilar
 Pocovi Mieras, Miguel
 Tejedor Hernandez, Diego
 Mallen Perez, Miguel
 Alonso Karlezi, Alberto
 Reyes Leal, Gilbert
 Castillo Fernandez, Sergio
 Martinez Martinez, Antonio

<120> Method for detecting LDL receptor gene mutations associated with

<130> U 015859-4

<140> 10542937

<141> 2011-04-13

<150> ES200300206

<151> 2003-03-01

<160> 259

<210> 1

<211> 60000

<212> DNA

<213> homo sapiens

<220>

<221> gene

<223> rLDL

<220>

<221> gene

<223> n at position 35360 represents aau, aac or aat

<220>

<221> gene

<223> n at position 35361 represents aau, aac or aat

<400> 1

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